Squamous Cell Carcinoma of the Ovary

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Benign cystic teratoma is a very common ovarian lesion; and it commonly occurs during a woman's reproductive years and most often is benign. In approximately 1% to 2% of cases, however, it can undergo a malignant transformation with a very poor prognosis. This is especially the case when disseminated disease is present. Usually the associated malignancy is squamous cell carcinoma, and radical surgery is recommended.

An American Samoan woman was air-evacuated to Tripler Army Medical Center for further evaluation and therapy after having undergone an exploratory laparotomy and right ovarian cystectomy. Her pathology at the time of her initial procedure revealed a mature cystic teratoma with a malignant degenerative component. Her diagnostic evaluation upon arrival was unremarkable except for her physical exam and pelvic CT. She subsequently underwent a radical surgical procedure to include a surgical staging procedure, revealing disseminated squamous cell carcinoma with FIGO stage III disease.

Whereas malignant transformation of a benign cystic teratoma is a rare occurrence, a high index of suspicion should be maintained whenever a preoperative diagnosis is encountered; a radical surgical approach with en bloc resection should be employed. Adjuvant therapy with radiation or chemotherapeutic agents in general has not been shown to improve the outcome, especially in disseminated disease.

Benign cystic teratoma, also known as a dermoid cyst, is a common lesion of the ovary. Among the group of tumors referred to as germ cell tumors, it is the most common and probably accounts for approximately 25% of all ovarian tumors.[1] It is notable for occurring most commonly in women in their reproductive years, and also for the fact that it is very often bilateral 10% to 15% of the time.[1] Since it originates from totipotential cells that have the ability to differentiate into mature derivatives from all three embryonic cell layers, ectoderm, mesoderm, and endoderm, it often can be found to harbor hair, bone, teeth, skin, etc, upon macroscopic and microscopic evaluation. It is usually benign and usually requires simple excision without any adjuvant therapy, however, in approximately 1% to 2% of cases, it can undergo malignant transformation.[2-3]

In the literature, there has been only several hundred reported cases in which malignant transformation has occurred in the presence of dermoid cysts. These reports, usually found in older women, most often describe lesions confined to the ovary itself or lesions without any metastasis. However, we report a case in which this lesion was found to have metastasis throughout the peritoneum, ie, FIGO IIIC disease.

Case Report

A 47-year-old woman from American Samoa was transferred to Tripler Army Medical Center for staging and therapeutic evaluation. On December 30, 1993 in American Samoa, she had complained of a several-week history of lower abdominal pain and distension. The review of her systems was otherwise unremarkable, as was her past medical history, social history, or past surgical history. At the time of her exam, she was noted to have a large abdominopelvic mass, later found sonographically to be a large, loculated cyst. On January 31, 1994, she subsequently underwent an exploratory laparotomy and left ovarian cystectomy. The pathologic diagnosis of the large ovarian mass was "mature cystic teratoma with a squamous cell carcinoma component," and she was air-evacuated to Tripler Army Medical Center.

At Tripler Army Medical Center, a thorough diagnostic evaluation revealed a hematocrit of 33.9%; a CA-125, AFP, CEA, and quantitative HCG were all within normal limits; normal electrolytes; and normal liver function tests. Her electrocardiogram demonstrated a normal sinus rhythm. A flexible sigmoidoscopy revealed a normal colonic mucosa through 60 cm and her Pap test was within normal limits. Radiologic analysis was notable for a normal mammogram and chest x-ray, but a CT scan revealed: 1) soft tissue infiltration of the mesenteric fat with multiple discrete masses consistent with peritoneal carcinomatosis due to metastatic ovarian malignancy; 2) probable right ovarian teratoma; 3) probable bilateral lower lobe scarring with bronchiectasis, but cannot rule out a malignant infiltrate in the region.

On March 21, 1994, she underwent an exam under anesthesia, exploratory laparotomy, modified radical hysterectomy, right salpingo-oophorectomy, resection of mesenteric nodules, appendectomy, omentectomy, pelvic aspirates and washing, and a Smead-Jones closure. The findings at the time of surgery included, "...a mass (on exam under anesthesia) that appeared to go to the umbilicus; multiple adhesions between the anterior abdominal wall and the bowel; a large 8x6 cm mass involving the omentum, large bowel, and small bowel; multiple very small nodules arising from the small bowel; uterus densely adhesed [with] tumor extending up the left infundibulopelvic ligament and the left round ligament; tumor involving the right tube and ovary and right parametrium; and multiple other filmy adhesions between the liver and the diaphragm." She tolerated the procedure well and progressed through an uneventful postoperative course without complication. Prior to her discharge from the hospital, she was thoroughly counseled via a translator about

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her postoperative therapeutic options: to include adjuvant chemotherapy or no further intervention. She elected to return home in order to discuss the prospects of further therapy with her family and was discharged in stable condition on March 25, 1994 with instructions as to when to return for staple removal and other appropriate disposition.

Her pathologic evaluation was notable for a right pelvic peritoneal mass, multiple omental nodules and masses, multiple pelvic biopsies, and a sigmoid colon nodule, involved by "infiltrating, moderately differentiated squamous cell carcinoma" (Fig 1). However, pelvic aspirates, pelvic washings, diaphragmatic scrapings, an appendix, and a small bowel nodule were all free of disease.

Discussion

Benign cystic teratomas are among the most common ovarian tumors reported. They usually occur during the reproductive years and are most commonly unilateral. Since they are derivatives of all three germ cell layers, many different types of mature tissues can develop. In the rare instance where these tumors have a malignant transformation, the most common malignancy is squamous cell carcinoma.[5] However, a review of the literature reveals authors who report other types of malignancies in association with degeneration, ie, adenocarcinoma, melanoma, and osteosarcoma.[6-8] Moreover, another group has reported a squamous cell degeneration "...in which endometriosis is the favored origin."[9] Nonetheless, this discussion will be limited to squamous cell degeneration.

There are several potential origins for the squamous cells involved in this degenerative process. However, since epidermal cells are almost always found on histologic evaluation, they are probably at the root of the etiologic process.[2] Moreover, it is important to note that it is not the size of the lesion that contributes to the poor prognosis for patients in which malignant degeneration is found.[10] A literature review and meta-analysis conducted by Krumerman and Chung in 1977 compared tumor size and prognosis, and they conclude, "...there was no significant correlation between tumor size and subsequent course..."[10] To the contrary, the association with poor prognosis and indolence seems to be more closely associated with whether or not the tumor extends through the ovarian capsule.[2,9,12] Whereas patients with stage I disease have survival rates reported to be as high as 76% in some series,[3] stage III and stage IV disease "...have a uniformly bad outlook," with patients with FIGO stage II to IV having survival rates of slightly greater than 11%.[3] As it was stated by Ribeiro et al, "...stage I cases are the only survivors." Most series attribute "...direct continuity and peritoneal seeding..." as the main means of the spread of a tumor, although the finding in at least one case of spinal metastasis demonstrates that hematogenous spread probably also occurs in some instances.[11]

Finally, since malignant degeneration of these tumors occurs so rarely, it makes recommendations for therapy very difficult, and this difficulty is certainly reflected in the literature. In stage I tumors in which the disease was confined to the ovary, several series have realized favorable results with surgery alone or postoperative radiation therapy and/or chemotherapy.[3] Most authors agree that radio-chemotherapeutic modalities have made no significant impact in survival in patients with more advanced disease.[4,10,12] Ribeiro et al employed two commonly used chemotherapeutic regimens with no significant long-term response, ie, cisplatin, etoposide, and bleomycin (PEB), and vincristine, actinomycin D, and cyclophosphamide (VAC).[4] Nonetheless, as far as surgical therapy is concerned, the goal should be to remove as much of the diseased tissue as possible while avoiding cyst rupture even if this requires draining the cyst initially, since "...partial resection followed by postoperative radiation and chemotherapy does not seem to improve the outcome...[11] To this end, Pantoja et al champion radical surgery as the procedure of choice involving "...en bloc resection of the cyst with all the adherent viscera...", after an initial positive tumor margin of the cyst wall on intraoperative frozen section.[11] This radical surgical approach is also recommended by Amerigo et al.[2]

We present a case in which tumor had spread outside of the ovary and radical surgical therapy was performed. Most cases in which malignant squamous cell degeneration was found in association with a mature teratoma occurred in older patients and with disease that was contained within the ovary itself. It is relatively uncommon for these tumors to present with FIGO stage IIIC disease. Our patient was offered adjuvant radiochemotherapy as a possible form of postoperative treatment although she was also counseled that the benefits of such were as yet unproven. She returned to American Samoa in stable condition to discuss further therapy with her family.

Finally there are several conclusions that can be drawn from the aforementioned case and review, supported to a great extent by the literature, and which should come into play whenever these lesions are discovered. It is important that appropriate staging be undertaken whenever these lesions are present. Many authors recommend performing intraoperative frozen sections, and when positive for malignancy, a radical en bloc procedure should be performed, with the exception of a lymph node dissection. These lesions are most commonly found in older, postmenopausal women, however, in rare cases they also can be detected in younger women. Radiation therapy and/or chemotherapy has been shown to be of little benefit in improving the survival rate, especially in patients with advanced disease, and any use of them should be considered to be only experimental at best until further study can be undertaken. However, for patients with stage I disease, some authors have supported using a similar approach to that of similarly staged squamous cell carcinoma of the cervix with mixed results at best.[3] Next, whether or not the lesion has extended beyond the ovarian capsule is the most important prognostic indicator for long-term survival, ie, the more invasive, the worse the prognosis. Nonetheless, it goes

➤ *Continued on page 707*

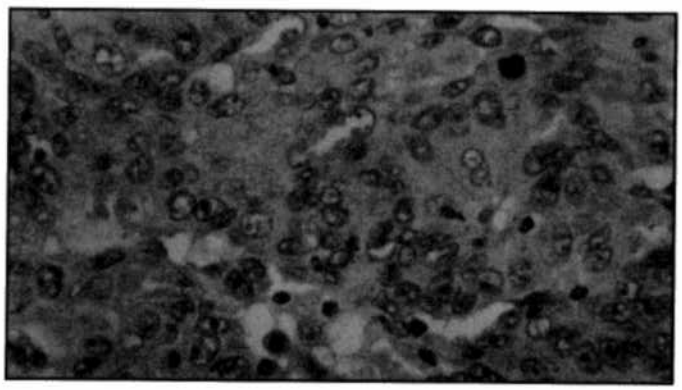

Fig 1.—Photomicrograph demonstrating a high-powered view of representative neoplastic squamous cells with irregular chromatin clearing, abnormal mitoses, increased nucleus-cytoplasmic ratio, and glassy eosinophilic cytoplasm.

7.5%=too high; A1C greater than 8.0%=urgent.

• Sulfonylureas starting doses: 1) Glyburide 2.5 mg, 2) Tolazamide 125 mg, 3) Glucotrol 5mg XL

–Increase dose to 1/2 the maximum dose, ie, Glyburide 5 mg bid; Tolazamide 250 mg bid; or Glucotrol XL 10 mg/d.

• Metformin: start with 500 mg before breakfast for 1 week; raise to maximum 500 mg ac 3 times a day.

• On failure of single agent (A1C 7.5% or greater) add second oral agent.

• When oral treatment fails, add evening dose of insulin to the oral agents.

1) For nonobese patients, give NPH insulin 5 to 10 units HS and increase gradually to achieve FBS less than 120.

2) For obese patients: use 10 units of insulin 70/30 before dinner and increase dose gradually: objective being A1C less than 8.0%.

• When no longer possible, consider multiple injections of insulin.

Squamous cell carcinoma of the ovary

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without saying that some generalities exist, and each case should be handled individually, including the patient and her family in the process, as was done in our case.

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